Use of Hospital Antibiograms as a Quality Indicator

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Abstract

Context: Antimicrobial susceptibility testing (AST) is a highly complex test in clinical laboratories. Prior to NCCLS M39-A publication in 2002, no guidance existed for standardized preparation of cumulative AST data (antibiograms).

Objective: To measure effectiveness of efforts to promote AST practice guidelines and determine if guidelines are being implemented in Michigan hospital laboratories by analyzing antibiograms submitted to Michigan Department of Community Health (MDCH) Bureau of Laboratories.

Methods: Clinical microbiology laboratories in Michigan were asked, on a voluntary basis, to submit antibiograms from years 2000 through 2003 to the Michigan Department of Community Health. Representative antibiograms were obtained from a total of 53 (48%) of 110 laboratories. Antibiograms were analyzed for unlikely resistance patterns, appropriateness of reported drugs and compliance with selected recommendations from M39-A. Errors found were categorized as major (reporting misleading or inappropriate organism/drug combinations, reporting impossible/ unlikely resistance patterns) or minor (misspelled organism names/antimicrobials, obvious math errors).

Results: Compliance with NCCLS M-39 A is increasing in some areas, and most errors are decreasing. Major errors decreased, from 56% of antibiograms in year 2000, to 18% of antibiograms in year 2003. Minor errors also decreased, from 13% in 2000, to 8% in 2003. The percentage of laboratories reporting *Streptococcus pneumoniae* data increased, from 75 % in 2000 to 88% in 2003, with an increase in dual breakpoint reporting noted. Forty-four percent of antibiograms from 2000 and 45% from 2003 presented data for organisms with <10 isolates, indicating this recommendation may be problematic, especially for smaller laboratories.

Conclusions: Laboratories may have difficulty implementing some recommendations in NCCLS M39-A. The decrease in major errors indicates that laboratories are increasing compliance with recommendations to verify unusual patient results before release. Further adoption of guidelines will provide more reliable data to clinicians to guide antibiotic choice.

Background

Antimicrobial Susceptibility Testing (AST) is highly complex testing, as categorized by the Clinical Laboratory Improvement Amendments (CLIA), and must be performed only by laboratories that fulfill all personnel and quality assurance requirements defined by CLIA for certification. The performance standards and interpretive guidelines for AST are defined by the Clinical and Laboratory Standards Institute (CLSI, formerly the NCCLS) through an evidence-based consensus process, with volunteer participants representing multiple constituencies. In addition to the performance and interpretive standards, in 2002 CLSI/NCCLS published the first guidance document (M39-A) for standardizing the statistical analysis of cumulative AST data by the clinical laboratory.

Despite lack of a consensus document prior to 2002, most hospital laboratories have long performed periodic statistical analysis of antimicrobial testing data. These cumulative antibiogram statistics are generally presented on an annual basis within a healthcare facility as the aggregate percentage(s) of organism(s) susceptible to various antibiotics on the hospital formulary, for the purpose of guiding empiric antimicrobial therapy before specific culture results are available on a particular patient. (See example in Figure 1.)

Hospital XYZ January 1 - December 31, 2001 Cumulative Antimicrobial Susceptibility Report	# Isolates	Ampicillin/amoxicillin	Ampicillin/sulbactam	Aztreonam	Cefazolin	Cefotaxime	Cefotetan	Ceftazidime	Ceftriaxone	Cefuroxime	Ciprofloxacin	Gentamicin	Imipenem	Levofloxacin	Piperacillin	Tetracycline	Ticarcillin/clavulanate	Tobramycin	Trimethoprim/sulfamethox
Gram-Negative																			
Enterobacter cloacae	32	13	34	82	3	74	58	78	78	50	100	100	100	100	78	92	74	100	100
Escherichia coli	577	68	69	99	96	96	99	99	99	97	98	96	100	96	74	82	95	99	86
Haemophilus influenzae	116	67	-	-	-	-	-	-	-	99	-	-	-	-	-	68	-	-	94
Klebsiella oxytoca	27	0	81	100	70	100	100	100	100	100	100	100	100	100	89	94	100	100	96
Klebsiella pneumoniae	106	6	87	100	99	100	100	100	100	93	99	100	98	99	86	91	98	100	96
Proteus mirabilis	56	91	88	100	84	95	98	100	96	89	98	98	98	100	91	4	98	98	95
Pseudomonas aeruginosa	144	-	-	75	-	-	26	92	27	-	81	74	91	78	95	-	90	97	-

%S for each organism / antimicrobial combination was generated by including the first isolate of that organism encountered on a given patient.
(-) Drug not tested or drug not indicated

Figure 1. Sample antibiogram

Highly complex and rapidly changing antimicrobial susceptibility testing (AST) requirements in response to emerging antimicrobial resistance present challenges to clinical laboratories. Clinical laboratories may also face economic barriers in complying with guidelines because CLSI/NCCLS AST interpretive standards are updated annually, test performance standards are updated every three years, and these copyright-protected documents must be purchased. To address these concerns, beginning in 2002 the Michigan Department of Community Health (MDCH) Bureau of Laboratories began offering educational programs on AST standards and guidelines. MDCH has also purchased the CLSI/NCCLS documents and provided them at no cost to sentinel (microbiology) laboratories in Michigan through a Cooperative Agreement with the Centers for Disease Control (CDC).

Objective

To measure effectiveness of efforts by MDCH Bureau of Laboratories to promote the CLSI/NCCLS performance/interpretive standards and antibiogram guideline; and to determine whether changes in the standards are being implemented in clinical laboratories by analyzing antibiograms from years 2000, 2001, 2002, and 2003.

Methods

Approximately 110 laboratories in Michigan perform antimicrobial susceptibility testing (1). MDCH asked these clinical laboratories to submit their antibiograms from years 2000, 2001, 2002, and 2003 on a voluntary basis to the MDCH Bureau of Laboratories. Antibiograms were requested each year via the MDCH quarterly newsletter and through direct fax requests. Laboratories were assured that anonymity would be maintained. No additional follow up or telephone request, etc. was attempted; however, 2003 antibiogram data was requested as a condition of enrollment in MDCH's 2004 sentinel laboratory preparedness program.

Antibiograms were analyzed for unlikely resistance patterns, appropriateness of reported drugs and compliance with selected recommendations from CLSI/NCCLS standards M2-A8, M7-A6, and guideline M39-A (2,3). Errors found were categorized as major (reporting unlikely/ impossible resistance patterns, reporting misleading or inappropriate organism/drug combinations) or minor (misspelled organism names/antimicrobials, obvious math errors).

Results

The number of antibiogram submissions increased each year. Antibiogram data was submitted by 19 laboratories in 2000, 29 in 2001, 41 in 2002, and 45 in 2003. Some laboratories submitted summary "raw" data printouts from automated instruments. For this QA analysis, only antibiograms submitted in "released" format were included. Sixteen usable antibiograms were received from 2000, 26 from 2001, 33 from 2002, and 40 from 2003. A total of 53 laboratories submitted 115 usable antibiograms: 18 submitted data from one year only, 13 from two years, 17 from three years, and 5 submitted antibiogram data from all four years. See Tables 1 and 2.

Year	Total # Labs submitting data	# Labs submitting Raw Data	# Labs submitting Released Data
2000	19	3	16
2001	29	3	26
2002	41	8	33
2003	45	5	40

Table 1. Number of usable antibiograms submitted per year

Year(s) data submitted	Number of labs	Number of antibiograms
1	18	18
2	13	26
3	17	51
4	5	20
Total	53	115

Table 2. Antibiograms submitted for one or more years

Major errors (defined as unlikely or impossible resistance patterns, or the reporting of misleading or dangerous organism/antimicrobial combinations) occurred each year but are decreasing. Fifty-six per cent of antibiograms from 2000 contained one or more major errors, 42% from 2001, 33% from 2002, and 18% from 2003 (Figure 2). Table 3 summarizes the percentage of antibiograms with major errors, and Table 4 lists the number and type of major errors found.

Major Errors	2000	2001	2002	2003
Unlikely or impossible resistance patterns	44%	38%	30%	16%
Misleading or dangerous combinations	13%	12%	6%	0
Total percentage of antibiograms with >= 1 major error(s)	56%	42%	33%	18%

Table 3. Percentage of antibiograms with major errors, years 2000-2003

	Gram Positive Organisms	2000	2001	2002	2003
Unlikely or impossible patterns	*S. aureus* <100% S to vancomycin	1	4	2	4
	MRSA (methicillin-resistant *Staphylococcus aureus*) >0% S to Beta-lactam		5		1
	Beta hemolytic *Streptococcus* <100% S to penicillin	2	4	2	
	Beta hemolytic *Streptococcus* <100% S to vancomycin		1	1	
	S. pneumoniae <100% S to vancomycin			1	1
Misleading or dangerous combinations	Cephalosporin reported on *Enterococcus*	1	1		
	Oxacillin reported on *S. pneumoniae*		2	2	
	Clindamycin reported on *Enterococcus*		1		
	SXT/TMP reported on *Enterococcus*		1		
	Gentamicin reported on *Enterococcus***		3**	1**	3**
	Quinupristin-dalfopristin reported on *Enterococcus* other than *E. faecium***	1**	1**	1**	5**
	Gram Negative Organisms	**2000**	**2001**	**2002**	**2003**
Unlikely or impossible patterns	*Pseudomonas aeruginosa* >0% S to ampicillin	2	1	3	2
	Enterobacter spp. 100% S to cefazolin	1			
	Haemophilus influenzae R to 3rd generation cephalosporin	3	5	4	1
Misleading or dangerous combinations	Cephalosporin reported on *Shigella* spp.	1			
	Aminoglycoside reported on *Shigella* spp.	1			
	Total Number of Major Errors	12	25	15	9

**** Excluded from analysis: see discussion** S = susceptible; R =resistant; SXT/TMP = sulfamethoxazole/trimethoprim;
***Note:** Total percentage does not equal the sum because some antibiograms contained more than one type of major error.

Table 4. Number and type of major errors each year from 2000-2003

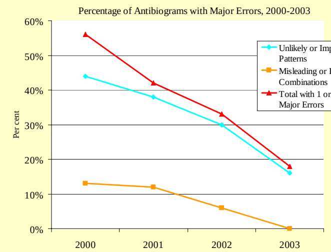

Figure 2. Major errors in antibiograms, years 2000-2003

Minor errors also decreased, from 13% in 2000 to 8% in 2003. Minor errors were defined as misspelled organism names or antimicrobials, and obvious math errors. For example, one antibiogram reported rifabutin, an anti-mycobacterial agent, instead of rifampin. An example of one obvious math error was the reporting of 10 isolates of a particular species, of which 14% were susceptible to an antimicrobial. Minor errors are summarized in Table 5. Table 6 lists the percentage of antibiograms with minor errors.

Minor Errors	2000	2001	2002	2003
Misspelled organism/antimicrobial	1	4	3	3
Obvious math error	1	2	0	0

Table 5. Number and type of minor errors each year from 2000-2003

Minor Errors	2000	2001	2002	2003
Misspelled organisms/antimicrobial	6%	15%	9%	8%
Obvious math error	6%	8%	0	0
Total percentage* of antibiograms with >=1 minor error(s)	13%	19%	9%	8%

Table 6. Percentage of antibiograms with minor errors, years 2000-2003

MDCH also examined antibiograms for compliance with four recommendations from the CLSI/NCCLS M39-A as one measure of how easily laboratories are able to adopt new guidelines:

- Indicating the inclusive dates used to create the cumulative report
- Analysis and inclusion of only species for which there are a minimum of ten isolates
- Reporting of susceptibility data on *Streptococcus pneumoniae*, and
- Elimination of duplicate isolates and inclusion of only the first isolate per patient, regardless of susceptibility pattern.

Inclusive dates used to create the report were indicated on 63 % of antibiograms from 2000, 69% from 2001, 55% from 2002, and 58% from 2003. Inclusion of only species for which the laboratory had more than ten isolates was noted in 56% of antibiograms from 2000, 58% from 2001, 61% from 2002, and 55 % from 2003.

Seventy-five percent of antibiograms reported *Streptococcus pneumoniae* data in 2000; 85% in 2001 and 2002; and 88% in 2003. Reporting of dual breakpoint data for *S. pneumoniae* has increased from 8% in 2001 to 45% in 2003. (The dual breakpoints were approved in 2001 for inclusion in the 2002 performance standards.)

Inclusion of only the first isolate per patient was evident on less than 10% of the antibiograms for any year.

These findings are summarized in Table 7.

Year	2000	2001	2002	2003
	Number of antibiograms / percent			
Dates of analysis included	10 63%	18 69%	18 55%	23 58%
Data calculated for species with >10 isolates only	9 56%	15 58%	19* 61%	22 55%
First isolates only included	0	1 4%	0	3 8%
Streptococcus pneumoniae data reported	12 75%	22 85%	28 85%	35 88%
Streptococcus pneumoniae dual (CSF/non-CSF) breakpoints reported for ceftriaxone/cefotaxime	0	2 8%	6 18%	18 45%

Table 7. Compliance with selected CLSI/NCCLS M39-A recommendations

Discussion

Laboratories should verify each patient result before reporting. As an example, Michigan reported two of four confirmed cases of vancomycin-resistant *Staphylococcus aureus*, the first known case in 2002 and the fourth in 2005. However, according to antibiogram data, one laboratory in 2000, four laboratories in 2001, one laboratory in 2002, and four laboratories in 2003 reported *Staphylococcus aureus* <100% susceptible to vancomycin.

It is possible that the laboratories repeated testing on these unusual isolates, the results did not confirm, and the vancomycin resistance was not reported on any patient. Because antibiogram data in some laboratories is derived from the automated testing instrument instead of the laboratory computer information system, if the original incorrect results were not deleted from the automated instrument data, they may have been included in the cumulative statistical analysis. This could account for these anomalies.

Other unusual resistance patterns were noted in the antibiograms. Beta-hemolytic streptococci that are non-susceptible to penicillin or vancomycin have not been reported in the literature to date. *Pseudomonas aeruginosa* susceptible to ampicillin, and *Enterobacter* species 100% susceptible to cefazolin are very unlikely. However, these patterns were also reported by a few laboratories. (see Table 4).

Because cumulative antibiograms are distributed to physicians to guide empiric therapy, MDCH also examined whether inappropriate antimicrobials were reported. Beginning in 2003, the NCCLS/CLSI documents included tables of unlikely resistance patterns and warnings of misleading or inappropriate antimicrobial organism combinations. (For example, for *Enterococcus* species, cephalosporins may appear susceptible *in vitro*, but they are not effective clinically and should not be reported.) MDCH examined the antibiograms for the combinations listed in NCCLS/CLSI standards, and the results are shown in Table 4.

Many laboratories reported gentamicin on *Enterococcus* species, which is not recommended. However because these are internal documents within an institution, it is likely that internal users understand that the cumulative gentamicin statistics indicate screening for high-level genatmicin resistance (recommended by CLSI/NCCLS) and not routine susceptibility results. These "errors" were not included in the analysis.

Quinupristin-dalfopristin is not appropriate for treating enterococci other than *E. faecium*, and NCCLS/CLSI recommends reporting this drug only on *E. faecium.* However, a few laboratories reported it as 0% susceptible for other Enterococcus species, possibly as a point of physician education, and this "error" was also excluded from the statistical analysis.

The errors noted in laboratory antibiograms prompted MDCH Bureau of Laboratories to focus educational efforts on recognition of unusual resistance, and the importance of verifying each patient result before releasing the laboratory report. These topics were incorporated into regional all-day workshops and sentinel laboratory update meetings. Reporting of misleading or dangerous combinations for 2002 data decreased by 50%, and none were noted on the antibiograms prepared from 2003 data.

Minor errors may not have a significant impact, they could perhaps indicate lack of oversight in the preparation of an antibiogram and thus were noted.

Thirty-one to 45% of antibiograms failed to include the dates of analysis. This finding is puzzling, and may reflect the fact that many laboratories had already established a familiar, albeit non-standardized template for their antibiograms. Most laboratories that did not include the actual dates did state that the antibiogram was from "2002 data", for example.

Including only species for which there are at least ten isolates during the period of analysis appeared to be problematic for some laboratories, although more than 50% were able to meet this recommendation. Some of the laboratories analyzed data quarterly or semi-annually. NCCLS/CLSI M39-A recommends an annual presentation of cumulative data; and if laboratories switch to yearly analysis, they will likely have a lower number of species with fewer than 10 isolates per year.

Capability of the various laboratory information systems and automated instruments to exclude duplicate isolates in a twelve month period varies considerably; and inclusion of only the first isolate per year per patient presents a major challenge for most laboratories. Fewer than 10 per cent of laboratories indicated on the antibiogram that duplicate isolates had been excluded, and even fewer defined what constituted exclusion of duplicate isolates.

Presentation of *Streptococcus pneumoniae* data was chosen as a quality indicator because of emerging antimicrobial resistance and changes in the interpretive criteria for susceptibility testing. Most laboratories (75-88%) report *S. pneumoniae* data. In 2002, NCCLS/CLSI began using different breakpoint criteria for the interpretation of susceptibility testing results for isolates of *S. pneumoniae* from meningitis vs. those from non-meningitis. Laboratories adopting this recommendation increased from 18% in 2002 to 45% in 2003.

Conclusion

- Laboratories are often surveyed about their testing practices, but analysis of antibiograms may be a useful tool to measure whether laboratories are incorporating changes and updates at the bench.
- Analysis of antibiograms may provide useful information when deciding where to focus educational efforts.
- Providing antibiogram data to public health agencies does not create more work for laboratories, as the data is already prepared for another purpose. However, there may be reluctance to share with public health what has been largely regarded within the hospital as proprietary data.
- Increased compliance with CLSI/NCCLS standards and guidelines, particularly those with regard to daily verification of unusual or unlikely results, should result in decreased errors on antibiograms, and thus provide more reliable data to clinicians to guide antibiotic choice.
- Programs that provide and explain the AST standards and guidelines may encourage compliance.

References

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